REMARKS

1. Amendments to the Claims

Claims 1, 4, 6-11 and 13-27 are pending. Claim 1 is herein amended to recite "said particle lacks a coating". Support for this amendment can be explicitly found in the Specification on page 21, lines 7-11. Implicit support for the lack of a coating can be found in the Specification in Example 1, page 29, lines 10 to page 30, line 4. Further support for the inherency of the lack of coating in view of the method of preparation of the particle can be found in the attached Declaration of Dr. Shimono, page 2 point 6 and the attached photographs. Claim 27 is herein amended. Support for the amendment to claim 27 can be found in the Specification at page 23, last paragraph.

No new matter has been added.

2. Claim Rejections

a. Written Description

The Examiner rejects claims 26 and 27 under 35 U.S.C. § 112, first paragraph as failing to comply with the written description requirement. The Examiner suggests that one of skill in the art was not in possession of a particle consisting of the medicament, methylcellulose, and mannitol in their particular amounts, which also includes a binder and/or fluidization agent (claim 26) or 1-4 ingredients selected from the group consisting of a binder, a fluidization agent, a corrigent, and a disintegrant (claim 27).

The Examiner acknowledges that page 21 generally discusses the binder, fluidization agent, corrigent, and disintegrant, but is concerned that none of the Examples describe a medicament containing a particle consisting of the ingredients of claim 26 or claim 27.

Applicants disagree with the Examiner, because "a patent claim is not necessarily invalid for lack of written description just because it is broader than the specific examples disclosed." *Martek Biosciences Corp. v. Nutrinova Inc.*, 579 F3d 1363, 92 USPQ2d 1148, 1153 (Fed. Cir. 2009). See also, *Tex. Instruments, Inc. v. Int'l Trade Comm'n*, 805 F.2d 1558, 1563, 231 U.S.P.Q. 833 (Fed. Cir. 1986) ("This court has cautioned against limiting the claimed invention to preferred embodiments or specific examples in the specification."). The proper test is whether a patent specification describes the claimed invention in sufficient detail that one skilled in the art can reasonably conclude that the inventor had possession of the claimed invention. *See, e.g., Moba, B.V. v. Diamond Automation, Inc.*, 325 F.3d 1306, 1319, 66 USPQ2d 1429, 1438 (Fed. Cir. 2003); *Vas-Cath, Inc. v. Mahurkar*, 935 F.2d at 1563, 19 USPQ2d at 1116.

Applicants submit that the Specification presents adequate evidence that Applicants had possession of a particle consisting of (1) a medicament with an unpleasant taste, (2) methylcellulose, (3) mannitol, and (4) a binder and/or fluidization agent and a particle consisting of (1) a medicament with an unpleasant taste, (2) methylcellulose, (3) mannitol, and (4) 1 to 4 ingredients selected from the group consisting of a binder, a fluidization agent, a corrigent and a disintegrant. Page 21, lines 12-15 of the Specification state "[t]he medicament-containing particle of the invention may further include corrigents, fluidization agents, ... [and] disintegrants... etc in the particle." Thus there is explicit disclosure of the presently claimed embodiment, and Applicants are not required to have a specific working example.

The Specification continues on to point to specific examples of each of the types of ingredients which can be used (Specification, page 21, lines 15-17 "These ingredients are exemplified in the following solid preparation which can be used as the above ingredients." Binders are exemplified on page 22, lines 21-25. Disintegrants, fluidization agents, and corrigents are exemplified on page 23, lines 1-21).

Applicants submit that they have demonstrated that the core ingredients (*i.e.*, the medicament, mannitol, and methylcellulose) of the claimed particles generate the taste-masking effect, and

that additional ingredients such as the specified binders, corrigents, fluidization agents, and disintegrants would not be expected to alter the fundamental taste-masking effect of the three ingredients. Accordingly Applicants request that the rejection be withdrawn.

b. Indefiniteness

The Examiner rejects claim 27 under 35 U.S.C. § 112, second paragraph, suggesting that claim 27 is indefinite because the term "corrigent" is not defined. The Specification at page 21, lines 12-17, state that "these ingredients [including corrigents] are exemplified in the following solid preparation, which can be used as the above ingredients." On page 23, lines 18-21, the Specification names certain specific corrigents which have been added to claim 27. Accordingly, Applicants submit that the claim is clear and request that the rejection be withdrawn.

c. Obviousness

Siebert

On page 4, point 9 of the Office Action, the Examiner rejects claims 1, 4, 6-7, 11, 13-20, and 22-24 under 35 U.S.C. § 103(a), as being unpatentable over Siebert (U.S. 6,368,625, of record).

On page 14, lines 18-22 of the Office Action the Examiner states:

> [I]n regards to the declaration that the tastemasking is present with the mannitol, methylcellulose, and drug with the ratios such that it is not necessary to use special techniques such as coating and microcapsulation, this is reconsidered and is persuasive but is not commensurate in scope with the claims as written and requires additional evidence. (emphasis added)

Applicants note that the claims have been amended to recite that the particle is uncoated. Applicants maintain that such a particle is taught by the Specification on page 21, lines 7-11 and page 2, lines 12-15 and lines 21-25. Implicit support for the lack of a coating can be found, for example, in the Specification in the Examples, such as Example 1, page 29, line 10 to page 30,

line 4 (where mosapride citrate, methylcellulose, and D-Mannitol were mixed and granulated with water, no coating material or step is added prior to the taste test).

In addition, Applicants herein provide further evidence that the particles of the claimed invention are not coated, either explicitly, implicitly, or inherently. In the attached Declaration of Dr. Shimono, mosapride citrate, methycellulose, D-Mannitol, and a binder (aqueous hydroxypropylcellulose) were mixed and granulated to make particles falling within the scope of the claims (see paragraph 6 on page 2 of the Declaration). The Declaration visually demonstrates that the particles are not coated, and that the mosapride citrate is on the surface of the particle. (See page 3, paragraph 10, and page 3, paragraph 12 of the Declaration, and the corresponding figures 1, 5, and 6.) Moreover, the Declaration visually demonstrates that the particles have a homogeneous mixture of the ingredients on the surface. (See page 3, paragraph 10, and figure 5 of the Declaration.)

Applicants submit that as the claims recite that the particles are uncoated, because the unexpected taste-masking effect of these uncoated particles is demonstrated in the Specification, and the Examiner acknowledges that an uncoated particle that exhibits taste-masking is patentably distinguishable over the prior art, the presently claimed particles are patentable over the prior art. Applicants respectfully request that the Examiner withdraw the current rejection.

The Examiner also states that "[a]ddressing the criticality of the ratios in addition [to evidence of the lack of coating] is also helpful." Applicants attach a summary of the Examples in the Specification which demonstrates that particles having the claimed ingredients in the claimed ratios (*i.e.* methylcellulose/medicament is 0.8-10 w/w and mannitol/methylcellulose is 0.3-12 w/w) have a significant improvement in taste compared to particles which have the claimed ingredients in ratios outside these ranges.

Specifically, looking at the table, all of the particles with ratios of ingredients (methylcellulose, D-mannitol, and mosapride citrate as the medicament) within the claimed range had a strong masking effect. Of the 17 examples having the three ingredients within the claimed range, 14 of

them (82.3%) have a "clearly exhibited" masking effect, and "the unpleasant taste was not felt at all." Three of the samples (17.6%) having ratios within the claimed ranges resulted in the effect that the "unpleasant taste was almost masked and was not actually felt."

In contrast, of the eight Examples which had ratios of ingredients outside the claimed range, none of them completely masked the taste of the unpleasant medicament. Furthermore, the masking effect of these particles was limited. Specifically, six of the Examples (75%) had a lesser masking effect than the lowest standard for the claimed particles *i.e.*, "the unpleasant taste was almost masked and was not actually felt."

Thus, the evidence already in the Specification clearly demonstrates that particles having ratios of ingredients within the claimed ranges have a significantly more effective taste-masking ability. Applicants submit that such evidence further demonstrates the importance of the ranges of the ingredients, such that one of skill in the art reviewing the cited references would have no expectation of success in achieving this heightened taste-masking ability. For this additional reason, Applicants request that the rejection be withdrawn.

***Siebert, Depui, and Yoshinari* (and *Shirai*)**

On page 6, point 10, the Examiner rejects claims 8-10 and 21 under 35 U.S.C. § 103, as being unpatentable over Siebert, in view of Depui (U.S. 6,132,771, of record) and further in view of Yoshinari (U.S. 6,235,947, of record). Applicants respectfully traverse.

The Examiner applies Depui for the teaching of mosapride. (Office Action, page 6.) The Examiner applies Yoshinari for the teaching of mannitol as an excipient for pharmaceutical compounds. (Office Action, page 7.) Neither of these teachings overcome the deficiencies of Siebert, *i.e.*, that one of skill would have expected that a particle would have to be coated to provide a taste-masking effect, and that the ranges of the ingredients are critical. Therefore, for at least the reasons discussed above with Siebert, Applicants request that the rejection be withdrawn.

Debregeas and Nishii

On page 8, point 11, the Examiner rejects claims 1, 4, 6-7, 11, 13-15, 17-20, 22-24, and 26-27 under 35 U.S.C. § 103, as being unpatentable over Debregeas (U.S. Patent Publication 2004/081691, hereinafter "Debregeas") in view of Nishii (U.S. 6,517,870, hereinafter "Nishii").

Applicants first point out that the structure of the particles in Debregeas is different from that of the claimed invention of claims 1, 4, 6-7, 11, 13-15, 17-20, 22-24, and 26-27. Debregeas describes a layered particle with neutral core granules which are subsequently coated with a plant substance which may optionally include a binder. (Debregeas, [0003].) Optionally, the neutral core/plant material coated granules can be coated. (*Id.*, [0012].) The granules are subsequently packaged in a gelatin capsule. (*Id.*, [0006].)

Debregeas does not mix and granulate mannitol with the active ingredient as discussed in the present claims (in particular the process claim 20). Debregeas relies on coating the neutral core particle with the medicament with an unpleasant taste. However, in the presently claimed particles, the mixed particle containing the medicament, methylcellulose and mannitol is uncoated (claims 1, 4, 6-7, 13-15, 17-19, 22-24, and 26-27). Debregeas does not disclose this feature, and the polyvinylpyrrolidone the Examiner would have substituted with methylcellulose to provide all of the ingredients of the claims is used as a coating. Thus, one of skill in the art following the logic of the Examiner would have no reason to 1) leave the particles uncoated, and 2) use methylcellulose in the particles. Because the combination of Debregeas with Nishii fails to teach every element of the claimed particles or the claimed process, Applicants submit that the rejection fails. Applicants request that it be withdrawn.

In addition, as demonstrated by the Shimono Declaration at figure 5, the present particles are a homogeneous mixture of mannitol, medicament, and methylcellulose. This is in sharp contrast to the layered structure taught by Debregeas. Accordingly, Applicants submit that they have provided sufficient evidence to establish that the process by which the claimed products are

made generates a completely different particle structure than that disclosed in the cited references. For this additional reason, Applicants request that the rejection be withdrawn.

Furthermore, Applicants emphasize that both ingredients, mannitol and methylcellulose, must be present to obtain the taste masking effect. The Examiner admits that Debregeas does not teach methylcellulose. The Examiner uses Nishii to suggest that one of skill in the art would have substituted methylcellulose for PVP. Applicants submit that the taste-masking effect obtained with the present invention is an *unexpected result* in comparison to the combined disclosures of Debregeas and the other references. If, as the Examiner's logic suggests, PVP is a functional equivalent of methylcellulose, it would be expected to also have similar taste masking abilities. The Specification indicates that "the desired effect could not be obtained when using the other water soluble polymer which is used for known granulation, such as . . . polyvinylpyrrolidone." (Specification, page 18, lines 9-13.) The Specification also describes in Table 8 (page 38), and Table 15 (page 47), in Comparative Example 9, that a composition which substitutes polyvinylpyrrolidone did not mask the unpleasant taste of the medicament in either particle or tablet form. Thus, the superior taste-masking ability of methylcellulose is unexpected.

Alkire

On page 10, point 12, the Examiner rejects claims 1, 4, 6-7, 11, 13-20, and 22-27 under 35 U.S.C. § 103, as being unpatentable over Alkire (U.S. 5,607,697, hereinafter "Alkire").

Like Debregeas above, Alkire requires a coating (col. 2, line 64-col. 3, line 1). Thus, Alkire already does not teach a feature of the claims, and the rejection should be withdrawn.

Also, Alkire teaches the inclusion of a binder, using polyvinylpyrrolidone as an example. (Alkire, col. 11, Table 1, col. 13, table 4.) Alkire discloses that methylcellulose can also be used as a binder but does not provide an example of its use. (Alkire, col. 6, lines 49-54.) The Examiner suggests that one of skill in the art would have substituted methylcellulose for polyvinylpyrrolidone (PVP). (Office Action, page 10.) However, as discussed above, the

particles do not show the unexpectedly superior taste-masking effects if PVP is used. Accordingly, Applicants submit that the claimed particles are not obvious in view of Alkire.

The Examiner also states that the amounts of the various ingredients are not disclosed, but one of skill would find them obvious based on the Alkire reference. However, as discussed above, the ranges of the claimed ingredients significantly contribute to the taste-masking ability of the resultant particles. Accordingly, one of skill in the art would not expect superior taste-masking effects based on the Alkire reference, and would have no indication of what ranges would generate the superior taste-masking abilities. For this additional reason, Applicants submit that the claimed invention is not obvious over Alkire. Applicants request that the rejection be withdrawn.

Alkire, Depui, MIMS, Yoshinari

On page 11, point 13, the Examiner rejects claims 8-10, and 21 under 35 U.S.C. § 103, as being unpatentable over Alkire in view of Depui, MIMS (Gasomotin®, hereinafter MIMS), and Yoshinari.

The teachings of Depui and Yoshinari are discussed above. The Examiner uses the MIMS reference to suggest that it was known that mosapride citrate is bitter tasting.

However, the assertion of Depui, Yoshinari, and MIMS fails to remedy the deficiencies of Alkire discussed above. They do not teach that the particles should be uncoated and they do not teach that the inclusion of methylcellulose in a particle would lead to a superior taste-masking effect. Accordingly, Applicants request that the rejection be withdrawn.

Applicants submit that the present application claims subject matter free of the prior art. The favorable actions of withdrawal of the standing rejections and allowance of the pending claims are requested.

Should there be any outstanding matters that need to be resolved in the present application, the Examiner is respectfully requested to contact Mark J. Nuell Reg. No. 36,623, at the telephone number of the undersigned below, to conduct an interview in an effort to expedite prosecution in connection with the present application.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies to charge payment or credit any overpayment to Deposit Account No. 02-2448 for any additional fees required under 37.C.F.R. §§1.16 or 1.14; particularly, extension of time fees.

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Respectfully submitted,

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Attachments: Request for Continued Examination
Amendment Transmittal Letter
Declaration of Dr. Shimono
Summary Table of Experiments
Petition for Extension of Time
Fee Transmittal